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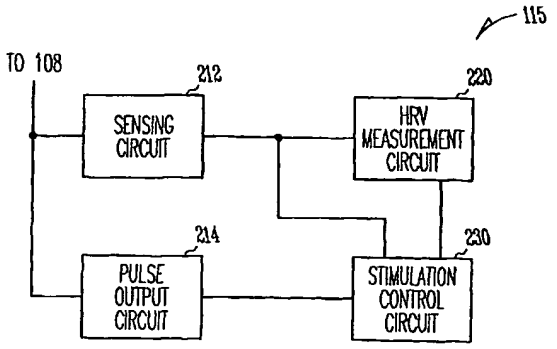
(54) Title: CONTROL OF ELECTRICAL STIMULATION USING HEART RATE VARIABILITY



(57) Abstract: A cardiac rhythm management system modulates the delivery of pacing and/or autonomic neurostimulation pulses based on heart rate variability (HRV). An HRV parameter being a measure of the HRV is produced to indicate a patient's cardiac condition, based on which the delivery of pacing and/or autonomic neurostimulation pulses is started, stopped, adjusted, or optimized. In one embodiment, the HRV parameter is used to evaluate a plurality of parameter values for selecting an approximately optimal parameter value. In another embodiment, the HRV parameter is used to adjust a maximum tracking rate in an atrial tracking pacing mode. In another embodiment, the HRV parameter is used as a safety check to stop an electrical therapy when it is believed to be potentially harmful to continue the therapy.

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CONTROL OF ELECTRICAL STIMULATION USING HEART RATE VARIABILITY

Claim of Priority

Benefit of priority is hereby claimed to U.S. Patent Application Serial Number 11/037,308, filed on January 18, 2005, and U.S. Patent Application Serial Number 11/037,723, filed on January 18, 2005, and U.S. Patent Application Serial Number 11/037,039, filed on January 18, 2005, which applications are herein incorporated by reference.

Cross-Reference to Related Applications

This application is related to co-pending, commonly assigned, U.S. Patent Application No. 10/726,062, entitled "CARDIAC RHYTHM MANAGEMENT SYSTEM USING TIME-DOMAIN HEART RATE VARIABILITY INDICIA," filed on December 2, 2003, which is hereby incorporated by reference in its entirety.

Field of the Invention

This document generally relates to cardiac rhythm management (CRM) systems and particularly, but not by way of limitation, to such systems using heart rate variability (HRV) to control delivery of electrical stimulation pulses.

Background

The heart is the center of a person's circulatory system. It includes an electro-mechanical system performing two major pumping functions. The left portions of the heart draw oxygenated blood from the lungs and pump it to the organs of the body to provide the organs with their metabolic needs for oxygen. The right portions of the heart draw deoxygenated blood from the body organs and pump it to the lungs where the blood gets oxygenated. These pumping functions are accomplished by cyclic contractions of the myocardium (heart muscles). In a normal heart, the sinoatrial node generates electrical impulses called action potentials at a normal sinus rate. The electrical impulses propagate through an electrical conduction system to various regions of the heart to excite the myocardial tissues of these regions. Coordinated delays in the propagations

of the action potentials in a normal electrical conduction system cause the various portions of the heart to contract in synchrony to result in efficient pumping functions indicated by a normal hemodynamic performance. A blocked or otherwise abnormal electrical conduction and/or deteriorated myocardial tissue cause dysynchronous contraction of the heart, resulting in poor hemodynamic performance, including a diminished blood supply to the heart and the rest of the body. The condition where the heart fails to pump enough blood to meet the body's metabolic needs is known as heart failure.

Electrical stimulation therapies have been applied to restore functions of the electrical conduction system and reduce the deterioration of myocardial tissue. Their potential benefits to a patient are achieved or maximized when such therapies are adaptive to the patient's cardiac conditions and metabolic needs, both changing over time. In one example, delivering pacing pulses at a relatively high rate may satisfy the patient's instantaneous metabolic need for participating in an intense physical activity but result in further deterioration of myocardial tissue. In another example, an electrical therapy preventing further deterioration of myocardial tissue may significantly limit the patient's exercise capacity when the therapy is being delivered.

For these and other reasons, there is a need to modulate the delivery of cardiac electrical therapies based on the patient's changing needs and conditions.

Summary

A CRM system modulates the delivery of pacing and/or autonomic neurostimulation pulses based on HRV, which is the variance in cardiac cycle lengths over a predetermined period of time. An HRV parameter being a measure of the HRV is produced to indicate a patient's cardiac condition, based on which the delivery of pacing and/or autonomic neurostimulation pulses is started, stopped, adjusted, or optimized.

In one embodiment, a CRM system includes a pulse output circuit, a sensing circuit, an HRV measurement circuit, and a stimulation control circuit. The pulse output circuit delivers electrical stimulation pulses. The sensing circuit senses a cardiac signal. The HRV measurement circuit measures the HRV to produce an HRV parameter. The stimulation control circuit includes a stimulation parameter optimization module that adjusts at least one stimulation

parameter to an approximately optimal value based on the HRV parameter. The stimulation parameter optimization module includes a stimulation parameter generator, a pulse output controller, and a stimulation parameter selector. The stimulation parameter generator produces a plurality of parameter values for the stimulation parameter. The pulse output controller controls the delivery of the electrical stimulation pulses using the plurality of parameter values during a stimulation parameter optimization period. The stimulation parameter selector selects the approximately optimal value for the stimulation parameter from the plurality of parameter values. The approximately optimal parameter value corresponds to a maximum value of the HRV parameter measured for the stimulation parameter optimization period.

In one embodiment, an HRV-based stimulation parameter optimization method is provided. A stimulation parameter optimization period is started. A cardiac signal is sensed. A plurality of parameter values for at least one stimulation parameter are produced. Electrical stimulation pulses are delivered using the plurality of parameter values during the stimulation parameter optimization period. A variance in cardiac cycle lengths is measured over a predetermined period of time to produce at least one HRV parameter based on the cardiac signal sensed during the stimulation parameter optimization period. An approximately optimal value is selected for the stimulation parameter from the plurality of parameter values. The approximately optimal value corresponds to a maximum value of the HRV parameter measured during the stimulation parameter optimization period.

In one embodiment, a CRM system includes a pacing output circuit, a sensing circuit, an HRV measurement circuit, and a pacing control circuit. The pacing output circuit delivers pacing pulses. The sensing circuit senses a cardiac signal. The HRV measurement circuit measures the HRV to produce an HRV parameter. The pacing control circuit includes a pacing algorithm execution module and a maximum tracking rate (MTR) adjustment module. The pacing algorithm execution module controls the delivery of the pacing pulses by executing an atrial tracking pacing algorithm using pacing parameters including an MTR. The MTR adjustment module adjusts the MTR based on the HRV parameter.

In one embodiment, a method for operating a cardiac pacemaker is provided. A cardiac signal is sensed. A variance in cardiac cycle lengths over a predetermined period of time is measured based on the sensed cardiac signal to produce an HRV parameter. An atrial tracking pacing algorithm is executed to control pacing pulse deliveries. The atrial tracking pacing algorithm uses pacing parameters including an MTR. The MTR is adjusted based on the HRV parameter.

In one embodiment, a CRM system includes a sensing circuit, an HRV measurement circuit, a pulse output circuit, and a stimulation control circuit. The sensing circuit senses a cardiac signal. The HRV measurement circuit measures an HRV to produce an HRV parameter. The pulse output circuit delivers electrical stimulation pulses. The stimulation control circuit includes a stimulation algorithm execution module and a safety check module. The stimulation algorithm execution module controls the delivery of the electrical stimulation pulses by executing at least one stimulation algorithm. The safety check module stops the execution of the stimulation algorithm based on the HRV parameter.

In one embodiment, an HRV-based safety assurance method for electrical stimulation is provided. A cardiac signal is sensed. A variance in cardiac cycle lengths is measured over a predetermined period of time to produce an HRV parameter based on the sensed cardiac signal. Electrical stimulation pulses are delivered by executing at least one stimulation algorithm. The execution of the stimulation algorithm is stopped when the HRV parameter falls out of a safety window.

This Summary is an overview of some of the teachings of the present application and not intended to be an exclusive or exhaustive treatment of the present subject matter. Further details about the present subject matter are found in the detailed description and appended claims. Other aspects of the invention will be apparent to persons skilled in the art upon reading and understanding the following detailed description and viewing the drawings that form a part thereof, each of which are not to be taken in a limiting sense. The scope of the present invention is defined by the appended claims and their equivalents.

Brief Description of the Drawings

In the drawings, which are not necessarily drawn to scale, like numerals describe similar components throughout the several views. The drawings illustrate generally, by way of example, but not by way of limitation, various embodiments discussed in the present document.

FIG. 1 is an illustration of an embodiment of a CRM system and portions of an environment in which the CRM system is used.

FIG. 2 is a block diagram illustrating one embodiment of a stimulation system being part of the CRM system.

FIG. 3 is a block diagram illustrating one embodiment of a pacing system being part of the CRM system.

FIG. 4 is a block diagram illustrating one embodiment of a neurostimulation system being part of the CRM system.

FIG. 5 is a block diagram illustrating one embodiment of a pacing system including an HRV-based MTR adjustment system.

FIG. 6 is a flow chart illustrating one embodiment of a method for adjusting an MTR using an HRV parameter.

FIG. 7 is a block diagram illustrating one embodiment of a stimulation system including an HRV-based stimulation parameter optimization module.

FIG. 8 is a block diagram illustrating one embodiment of the stimulation parameter optimization module.

FIG. 9 is a block diagram illustrating another embodiment of the stimulation parameter optimization module.

FIG. 10 is a flow chart illustrating one embodiment of a method for stimulation parameter optimization using an HRV parameter.

FIG. 11 is a block diagram illustrating one embodiment of a stimulation system including an HRV-driven therapy switch system.

FIG. 12 is a flow chart illustrating one embodiment of a method for starting and stopping a therapy using an HRV parameter.

Detailed Description

In the following detailed description, reference is made to the accompanying drawings which form a part hereof, and in which is shown by way of illustration specific embodiments in which the invention may be

practiced. These embodiments are described in sufficient detail to enable those skilled in the art to practice the invention, and it is to be understood that the embodiments may be combined, or that other embodiments may be utilized and that structural, logical and electrical changes may be made without departing from the spirit and scope of the present invention. The following detailed description provides examples, and the scope of the present invention is defined by the appended claims and their equivalents.

It should be noted that references to "an", "one", or "various" embodiments in this disclosure are not necessarily to the same embodiment, and such references contemplate more than one embodiment.

This document discusses, among other things, a CRM system using a closed-loop system to control delivery of cardiac therapies based on a patient's HRV. HRV is known to indicate autonomic balance between the output of the parasympathetic and sympathetic nervous systems, thereby indicating the patient's cardiac condition. Generally, the patient's cardiac condition improves when HRV increases and worsens when HRV decreases. If the patient suffers left ventricular dysfunction, the autonomic balance shifts toward the sympathetic nervous system, and the HRV decreases. Thus, the closed-loop system modulates the cardiac therapies to increase or maximize the patient's HRV.

HRV is the beat-to-beat variance in cardiac cycle length over a period of time. An "HRV parameter" as used in this document includes any parameter being a measure of the HRV, including any qualitative expression of the beat-to-beat variance in cardiac cycle length over a period of time. In one embodiment, the HRV parameter is the time differences between successive cardiac cycle lengths averaged over a predetermined period of time. In one specific embodiment, the cardiac cycle lengths are ventricular cycle lengths, i.e., V-V intervals, or R-R intervals, which are time intervals between successive ventricular depolarizations (R waves). In an alternative specific embodiment, the cardiac cycle lengths are atrial cycle lengths, i.e., A-A intervals, or P-P intervals, which are time intervals between successive atrial depolarizations (P waves). In various specific embodiments, the HRV parameters includes, but are not limited to, Standard Deviation of Normal-to-Normal intervals (SDNN), Standard Deviation of Averages of Normal-to-Normal intervals (SDANN), ratio

of Low-Frequency (LF) HRV to High-Frequency (HF) HRV (LF/HF ratio), HRV footprint, and Root-Mean-Square of Successive Differences (RMSSD).

Standard Deviation of Normal-to-Normal intervals (SDNN). Normal-to-Normal intervals refer to R-R intervals during a normal sinus rhythm. SNDD is the standard deviation of the R-R intervals measured over a predetermined time period.

Standard Deviation of Averages of Normal-to-Normal intervals (SDANN). Normal-to-Normal intervals refer to R-R intervals during a normal sinus rhythm. To compute SDANN, R-R intervals are measured and averaged over a first time period. The standard deviation of the averaged R-R intervals is computed for a second time period that includes multiple first time periods. In one embodiment, measured R-R intervals are averaged over five-minute periods for 24 hours (i.e., 288 five-minute periods). The SDANN is the standard deviation of five-minute mean R-R intervals computed for the 24-hour period.

Ratio of LF HRV to HF HRV (LF/HF ratio). The LF HRV includes components of the HRV having frequencies between about 0.04 Hz and 0.15 Hz. The HF HRV includes components of the HRV having frequencies between about 0.15 Hz and 0.40 Hz. The LF/HF ratio is used to track trends in shifts of autonomic balance. A substantial change in the LF /HF ratio indicates a change in systemic stress that indicates the degree to which the sympathetic nervous system is over-stimulated.

HRV footprint. HRV footprint refers to a histogram of the HRV plotted against heart rate. The time difference between successive R-R intervals are determined for a period of time and plotted versus the heart rate measured over that period of time.

Root-Mean-Square of Successive Differences (RMSSD). Root-mean-square values are computed, each for time differences between successive R-R intervals determined for a period of time.

The HRV parameters discussed above are examples of HRV parameters used in the closed-loop system that modulates cardiac therapies to increase or maximize the patient's HRV. One of ordinary skill in the art will understand, upon reading and comprehending this document, that other parameters capable of representing or indicating the HRV can be used as the HRV, according to the present subject matter.

Some HRV parameters provide for relatively short-term measures of the HRV. Other HRV parameters for relatively long-term measures of the HRV. Certain HRV parameters are capable of providing both short-term and long-term measures of the HRV with reasonable accuracy. In one exemplary embodiment, a therapy is delivered to a patient with different predetermined values of one or more therapy parameters to evaluate the effects of the one or more therapy parameters. An HRV parameter is measured during the evaluation. The values of one or more therapy parameters that yield the most desirable HRV are selected as the optimal values for the patient. To limit the evaluation to a reasonable duration, a suitable HRV parameter provides reasonable accuracy when used as a short-term measure of the patient's HRV. In another exemplary embodiment, a therapy is delivered to a patient with one or more dynamically adjusted therapy parameters over a relatively long period of time, such as 24 hours. An HRV parameter is measured and recorded, with the values of the one or more therapy parameters applied, during that period of time. This results in a map relating the HRV parameters to the values of the one or more therapy parameters, which provides a basis for determining optimal therapy parameter values for the patient. In such an embodiment, a suitable HRV parameter provides reasonable accuracy when used as a long-term measure of the patient's HRV. In general, one of ordinary skill in the art will understand, upon reading and comprehending this document, that the selection of one or more particular HRV parameters depends on the overall design of the method and system for modulating cardiac therapies based on the HRV.

FIG. 1 is an illustration of an embodiment of a CRM system 100 and portions of an environment in which CRM system 100 is used. System 100 includes an implantable system 105, an external system 185, and a telemetry link 180 providing for communication between implantable system 105 and external system 185.

Implantable system 105 includes, among other things, implantable medical device 110 and lead system 108. In various embodiments, implantable medical device 110 is an implantable CRM device including one or more of a pacemaker, a cardioverter/defibrillator, a cardiac resynchronization therapy (CRT) device, a cardiac remodeling control therapy (RCT) device, a neruostimulator, a drug delivery device or a drug delivery controller, and a

biological therapy device. As illustrated in FIG. 1, implantable medical device 110 is implanted in a body 102. In various embodiments, lead system 108 includes leads for sensing physiological signals and delivering pacing pulses, cardioversion/defibrillation shocks, neurostimulation pulses, and/or pharmaceutical or other substances. In one embodiment, lead system 108 includes one or more pacing-sensing leads each including at least one electrode placed in or on a heart 101 for sensing electrogram and/or delivering pacing pulses. In another embodiment, lead system 108 includes one or more neurostimulation-sensing leads each including at least one electrode placed on a nerve of the autonomic nervous system for sensing neural signals and delivering neurostimulation pulses. In another embodiment, lead system 108 includes one or more pacing-sensing leads and one or more neurostimulation-sensing leads to synchronize neurostimulation with intrinsic activities of heart 101 and/or pacing.

In one embodiment, external system 185 is a patient management system including an external device 190, a network 192, and a remote device 194. External device 190 is within the vicinity of implantable medical device 110 and communicates with implantable medical device 110 bi-directionally via telemetry link 180. Remote device 194 is in a remote location and communicates with external device 190 bi-directionally via network 192, thus allowing a user to monitor and treat a patient from a distant location. In another embodiment, external system 185 includes a programmer communicating with implantable medical device 110 bi-directionally via telemetry link 180.

System 100 includes a stimulation system 115 that uses an HRV parameter for closed-loop control of stimulation pulse delivery. In one embodiment, implantable medical device 110 includes a pacemaker that delivers pacing pulses to heart 101 to maximize the HRV. In another embodiment, implantable medical device 110 includes a neurostimulator that delivers neurostimulation pulses to the autonomic nervous system to maximize the HRV. In another embodiment, implantable medical device includes a pacemaker and a neurostimulator to deliver combined cardiac pacing and autonomic neurostimulation to maximize the HRV. The distribution of stimulation system 115 in system 100 depends on design and patient management considerations, such as the size and power consumption of each system component and the ability of monitoring the patient in various settings from various locations. In

one embodiment, as illustrated in FIG. 1, implantable medical device 110 includes the entire system 115. This allows implantable system 105 to adjust stimulation parameters in response to changes in an HRV parameter without communicating to external system 185. In another embodiment, implantable medical device 110 and external system 185 each include portions of system 115. Stimulation parameters are adjusted based on an HRV parameter when implantable medical device 110 and external system 185 are communicatively coupled via telemetry link 180.

FIG. 2 is a block diagram illustrating one embodiment of stimulation system 115. Stimulation system 115 includes a sensing circuit 212, a pulse output circuit 214, an HRV measurement circuit 220, and a stimulation control circuit 230.

Sensing circuit 212 senses at least a cardiac signal that allows for a measurement of the HRV. In one embodiment, sensing circuit 212 senses one or more additional signals each indicative of one or more cardiac functions from the heart and/or the autonomic nervous system through one or more electrodes of lead system 108. Pulse output circuit 214 delivers electrical stimulation pulses to the heart and/or the autonomic nervous system through one or more electrodes of lead system 108. HRV measurement circuit 220 measures the HRV and produces at least one HRV parameter based on a signal sensed by sensing circuit 212. In various embodiments, HRV measurement circuit 220 includes, but is not limited to, one or more of an SDNN generator to produce an SDNN, an SDANN generator to produce an SDANN, an LF/HF ratio generator to produce an LF/HF ratio, an HRV footprint generator to produce an HRV footprint, and an RMSSD generator to produce an RMSSD. In one embodiment, HRV measurement circuit 220 includes an autonomic balance monitor to monitor an HRV parameter indicative of a balance between sympathetic and parasympathetic activities. In one specific example, the autonomic balance monitor includes the LF/HF ratio generator to produce the LF/HF ratio as the HRV parameter indicative of the balance between sympathetic and parasympathetic activities. Stimulation control circuit 230 controls the delivery of the electrical stimulation pulses from pulse output circuit 214 using one or more stimulation parameters that are adjusted or optimized based on the HRV parameter. In one embodiment,

stimulation control circuit 230 determines an approximately optimal value for each adjustable parameter that affects the HRV.

FIG. 3 is a block diagram illustrating one embodiment of a pacing system 315, which is a specific embodiment of stimulation system 115. Pacing system 315 includes a sensing circuit 312, a pacing output circuit 314, HRV measurement circuit 220, and a pacing control circuit 330.

Sensing circuit 312 is a specific embodiment of sensing circuit 212 and includes an electrogram sensing circuit. The electrogram sensing circuit senses one or more atrial and/or ventricular electrograms. Pacing output circuit 314 is a specific embodiment of pulse output circuit 214 and delivers pacing pulses to one or more atrial and/or ventricular sites. Pacing control circuit 330 is a specific embodiment of stimulation control circuit 230 and controls the delivery of the pacing pulses from pacing output circuit 314 using one or more pacing parameters that are adjusted or optimized based on the HRV parameter. In one embodiment, pacing control circuit 330 determines an approximately optimal value for each adjustable pacing parameter that affects the HRV. Examples of such adjustable pacing parameters include, but are not limited to, atrioventricular delays (AVDs), interventricular delays (IVDs), and pacing sites (sites to which the pacing pulses are delivered).

FIG. 4 is a block diagram illustrating one embodiment of a neurostimulation circuit 415, which is another specific embodiment of stimulation system 115. Neurostimulation system 415 includes a sensing circuit 412, a neurostimulation output circuit 414, HRV measurement circuit 220, and a neurostimulation control circuit 430.

Sensing circuit 412 is a specific embodiment of sensing circuit 212 and includes a neural signal sensing circuit in addition to an electrogram sensing circuit. The neural sensing circuit senses one or more neural signals from the autonomic nervous system including sympathetic and parasympathetic nerves. The electrogram sensing circuit senses one or more atrial and/or ventricular electrograms to allow for measurement of the HRV. In one embodiment, the one or more atrial and/or ventricular electrograms also allow for a delivery of neurostimulation that is synchronized to cardiac activities detectable from the one or more electrograms. Neurostimulation output circuit 414 is a specific embodiment of pulse output circuit 214 and delivers neurostimulation pulses to

one or more nerves of the autonomic nervous system. Neurostimulation control circuit 430 is a specific embodiment of stimulation control circuit 230 and controls the delivery of the neurostimulation pulses from neurostimulation output circuit 414 using one or more neurostimulation parameters that are adjusted or optimized based on the HRV parameter. In one embodiment, neurostimulation control circuit 430 determines an approximately optimal value for each adjustable pacing parameter that affects the HRV. Examples of such adjustable neurostimulation parameters include, but are not limited to, stimulation frequencies, stimulation amplitudes, and stimulation sites (sites to which the neurostimulation pulses are delivered).

In another specific embodiment, stimulation system 115 is a combination of pacing system 315 and neurostimulation system 415, and implantable medical device 110 is an implantable pacemaker-neurostimulator. In this embodiment, sensing circuit 212 combination of sensing circuits 312 and 412, pulse output circuit 214 is a combination of pacing output circuit 314 and neurostimulation circuit 414, and stimulation control circuit 230 is a combination of pacing control circuit 330 and neurostimulation circuit 430. In one embodiment, stimulation system 115 delivers pacing and neurostimulation pulses in a temporally coordinated manner to improve or optimize the HRV parameter.

In the following examples, specific embodiments of stimulation system 115, including pacing system 315, neurostimulation system 415, and the combination thereof, are discussed to illustrate, but not to restrict, the use of an HRV parameter for stimulation control according to the present subject matter.

EXAMPLE 1: HRV-Based Maximum Tracking Rate (MTR) Adjustment

A decreased HRV indicates that a patient has a worsened or worsening cardiac condition and should therefore limit exercise intensity. In a multi-channel (including dual-channel) pacemaker pacing in an atrial tracking mode (such as VDD or DDD mode), the ventricular pacing rate tracks the atrial rate up to a programmed maximum tracking rate (MTR). The MTR prevents the ventricles from being paced to a potentially harmful rate, for example, when atrial tachycardia or atrial fibrillation occurs. When a patient exercises, the sinus rate increases, and the atrial tracking mode pacing drives the ventricular rate to increase with the sinus rate within the limit set by the MTR. The increased

ventricular rate results in increased blood flow to the body to meet the patient's increased metabolic need for oxygen. If the MTR is set too high, when the patient's exercise intensity reaches a certain level, the pacing may allow the patient to continue or further increasing the intensity of exercise even when doing so puts the patient's heart at risk. If the MTR is adequately set, the ventricular rate stops increasing at an exercise intensity tolerable by the heart, and the patient feels the need to either stop exercising or stop increasing exercise intensity. Thus, an adequately set MTR prevents the pacing from providing the patient with an exercise capacity that is at a potentially harmful level. Because patient's cardiac condition including the tolerance to exercise changes over time, an MTR adjusted base on the patient's HRV is capable of maximizing benefits of pacing without causing harmful effects to the heart.

FIG. 5 is a block diagram illustrating one embodiment of a pacing system 515 including an HRV-based MTR adjustment system. Pacing system 515 is a specific embodiment of pacing system 315 and includes sensing circuit 312, pacing output circuit 314, HRV measurement circuit 220, and a pacing control circuit 530.

Pacing control circuit 530 includes an MTR adjustment module 532 and a pacing algorithm execution module 534. MTR adjustment module 532 adjusts an MTR based on an HRV parameter. In one embodiment, as illustrated in FIG.5, MTR adjustment module 532 includes an MTR selector 536 to select a value for the MTR from a plurality of predetermined values based on an HRV parameter produced by HRV measurement circuit 220. In one embodiment, a higher value and a lower value for the MTR and a threshold HRV level are determined for a patient based on the patient's cardiac condition. MTR adjustment module 532 receives the HRV parameter from HRV measurement circuit 220 and compares the HRV parameter to the threshold HRV level. MTR selector 536 sets the MTR to the higher value if the HRV parameter exceeds the threshold HRV level and the lower value if the HRV parameter does not exceed the threshold HRV level. In another embodiment, three of more substantially different values for the MTR and two or more threshold HRV levels are determined for a patient to provide a finer control of MTR based on the HRV parameter. In a further embodiment, MTR adjustment module 532 includes an HRV threshold generator to dynamically adjust the threshold HRV level(s)

based on an indication, estimation, or prediction of the patient's activity level. In one specific embodiment, the HRV threshold generator adjusts one or more threshold HRV levels based on the patient's heart rate. In another embodiment, the HRV threshold generator adjusts one or more threshold HRV levels based the patient's anticipated activity level during specific times of each day.

Pacing algorithm execution module 534 controls the delivery of pacing pulses from pacing output circuit by executing an atrial tracking pacing algorithm that uses the MTR. Pacing algorithm execution module 534 includes, but is not limited to, one or more of a bradycardia pacing algorithm execution module, a CRT pacing algorithm execution module, and an RCT pacing algorithm execution module. One of such pacing algorithm execution modules is activated to execute one of the pacing algorithms at an instant. In one embodiment, CRT pacing provides for an approximately optimal hemodynamic performance, and RCT pacing reduces the degree of post MI remodeling. In one embodiment, a CRT pacing algorithm is executed with one or more pacing parameters approximately optimized to maximize a measure of hemodynamic performance, for example, as a treatment improving quality of life for a heart failure patient. An RCT pacing algorithm is executed to reduce the degree of remodeling by redistributing the loading or stress on the LV wall, for example, as a post myocardial infarction (MI) treatment.

FIG. 6 is a flow chart illustrating one embodiment of a method for adjusting an MTR using an HRV parameter. In one embodiment, the method is performed by pacing system 515.

A cardiac signal is sensed at 600. The cardiac signal is indicative of cardiac depolarizations and allows for a measurement of the HRV. In one embodiment, the cardiac signal includes an atrial electrogram or a ventricular electrogram.

The HRV is measured based on the sensed cardiac signal, and at least one HRV parameter is produced based on the HRV measurement, at 610. In one embodiment, atrial depolarizations are detected from an atrial electrogram. Atrial intervals between successive atrial depolarization are measured. The HRV parameter is calculated based on the atrial intervals. In another embodiment, ventricular depolarizations are detected from a ventricular electrograms. Ventricular intervals between successive ventricular

depolarization are measured. The HRV parameter is calculated based on the ventricular intervals.

An atrial tracking pacing algorithm is executed to control a delivery of pacing pulses at 620. The atrial tracking pacing algorithm uses an MTR. Examples of the atrial tracking pacing algorithm include a bradycardia pacing algorithm, a CRT pacing algorithm, and a RCT pacing algorithm.

The MTR is adjusted based on the HRV parameter at 630. In one embodiment, the MTR is set to one of a plurality of predetermined values based on the HRV parameter. In one specific embodiment, the HRV parameter is compared to a threshold HRV level. The MTR is set to a first value if the HRV parameter exceeds the predetermined threshold HRV level and a second value if the HRV parameter does not exceed the threshold HRV level. The first value is substantially higher than the second value to allow for a higher exercise intensity when the HRV is higher. In one embodiment, the threshold HRV level is dynamically adjusted based on an indication, estimation, or prediction of the patient's activity level. In one specific embodiment, the threshold HRV level is adjusted based on the patient's heart rate. In another embodiment, the threshold HRV level is adjusted based the patient's anticipated activity level during specific times of each day.

EXAMPLE 2: HRV-Based Therapy Parameter Optimization

Because HRV is indicative of a patient's cardiac condition, an HRV parameter is capable of indicating effects of an electrical stimulation therapy including pacing therapy, autonomic neurostimulation therapy, and a combination of the pacing and autonomic neurostimulation therapies. To maximize the benefit of the therapy, therapy parameters are adjusted for the maximum HRV practically achievable by delivering electrical stimulation pulse to the patient's heart and/or autonomic nervous system.

FIG. 7 is a block diagram illustrating one embodiment of a stimulation system 715 that includes an HRV-based stimulation parameter optimization module. Stimulation system 715 is a specific embodiment of stimulation system 115 and includes sensing circuit 212, pulse output circuit 214, HRV measurement circuit 220, and a stimulation control circuit 730.

Stimulation control circuit 730 includes a stimulation parameter optimization module 731 that adjusts at least one stimulation parameter to an approximately optimal value based on at least one HRV parameter produced by HRV measurement circuit 220.

In one embodiment, stimulation control circuit 730 includes a pacing control circuit that includes a pacing parameter optimization module to adjust at least one pacing parameter to an approximately optimal value based on the HRV parameter. The pacing parameter optimization module includes, but is not limited to, one or more of an AVD optimization module to optimize an AVD, an IVD optimization module to optimize an IVD, and a pacing site optimization module to optimize a selection of one or more sites to which the cardiac pacing pulses are delivered. In general, the pacing parameter optimization module allows optimization of any pacing parameter whose value affects the HRV by adjusting that parameter for a maximum HRV indicated by the HRV parameter. In another embodiment, stimulation control circuit 730 includes a neurostimulation control circuit that includes a neurostimulation parameter optimization module to adjust at least one neurostimulation parameter to an approximately optimal value based on the HRV parameter. The neurostimulation parameter optimization module includes, but is not limited to, one or more of a stimulation pulse frequency optimization module to optimize a stimulation frequency and a stimulation sites optimization module to optimize a selection of one or more sites to which the neurostimulation pulses are delivered. In general, the neurostimulation parameter optimization module allows optimization of any neurostimulation parameter whose value affects the HRV by adjusting that parameter for a maximum HRV indicated by the HRV parameter.

In one embodiment, HRV measurement circuit 220 continuously updates the HRV parameter to reflect changes in the patient's cardiac condition, and stimulation parameter optimization module 731 adjusts the stimulation parameter to the approximately optimal value based on the HRV parameter on a continuous basis. In another embodiment, stimulation parameter optimization module 731 determines the approximately optimal value for the stimulation parameter based on the HRV parameter during a stimulation parameter optimization period. This period is started according to a predetermined schedule, such as on a programmed periodic basis, or is started in response to a

command, such as a command entered by a physician or other caregiver. Stimulation parameter optimization module 731 includes a stimulation parameter generator 738, a pulse output controller 740, and a stimulation parameter selector 742. Stimulation parameter generator 738 produces a plurality of parameter values for the stimulation parameter that is to be optimized. Pulse output controller 740 controls the delivery of electrical stimulation pulses using the plurality of parameter values during the stimulation parameter optimization period. Stimulation parameter selector 742 selects an approximately optimal value for the stimulation parameter from the plurality of parameter values. The approximately optimal value is the value corresponding to a maximum value of the HRV parameter obtained with pacing using the plurality of parameter values. Specific examples of stimulation parameter optimization module 731 that optimizes at least one stimulation parameter during a stimulation parameter optimization period are discussed below with reference to FIGS. 8 and 9.

FIG. 8 is a block diagram illustrating one embodiment of a stimulation parameter optimization module 831, which is one embodiment of stimulation parameter optimization module 731. Stimulation parameter optimization module 831 includes an optimization timer 846, a stimulation parameter generator 838, a pulse output controller 840, and a stimulation parameter selector 842. Stimulation parameter optimization module 831 determines an approximately optimal value for at least one stimulation parameter by delivering test stimulation pulses using a plurality of predetermined values for the stimulation parameter while measuring the HRV and selects the value for the stimulation parameter that corresponds to a maximum value of the HRV parameter. As one embodiment of stimulation parameter optimization module 731, stimulation parameter optimization module 831 is applicable for optimization of pacing parameters, neurostimulation parameters, or both.

Optimization timer 846 starts the stimulation parameter optimization period during which the test stimulation pulses are delivered and the approximately optimal value for the stimulation parameter is determined. In one embodiment, optimization timer 846 starts the stimulation parameter optimization period according to a predetermined schedule, such as on a periodic basis. In one embodiment, optimization timer 846 is programmed to start the stimulation parameter optimization period when the patient is at rest, such as

during sleeping time. In another embodiment, optimization timer 846 starts the stimulation parameter optimization period as requested by a person such as a physician, other caregiver, or the patient. The stimulation parameter optimization period ends when the approximately optimal value for the stimulation parameter is selected.

Stimulation parameter generator 838 produces the plurality of values for the stimulation parameter. In one embodiment, as illustrated in FIG. 8, stimulation parameter generator 838 includes a physiologic parameter measurement module 844 that measures at least one physiologic parameter related to the patient's cardiac condition. Examples of the physiologic parameter include the heart rate and a time interval between two detectable cardiac electrical and/or mechanical events. Stimulation parameter generator 838 produces the plurality of values for the stimulation parameter based on the measured physiologic parameter.

Pulse output controller 840 controls the delivery of stimulation pulses using the plurality of values produced for the stimulation parameter during the stimulation parameter optimization period. Pulse output controller 840 includes a stimulation algorithm execution module to control the delivery of stimulation pulses by executing a stimulation algorithm using the stimulation parameter. The stimulation algorithm is executed to control the delivery of a plurality of stimulation pulse series. Each stimulation pulse series includes a plurality of stimulation pulses to be delivered using one of the plurality of values produced for the stimulation parameter. In one embodiment, each stimulation pulse series is preceded by a non-stimulation period to establish a baseline HRV, such that the effect of stimulation for that stimulation pulse series can be substantially isolated. In various embodiments, the stimulation algorithm execution module includes one or more of a bradycardia pacing algorithm execution module, a CRT pacing algorithm execution module, an RCT pacing algorithm execution module, an autonomic neurostimulation algorithm execution module, and a combined pacing-neurostimulation algorithm execution module. One of such algorithm execution modules is activated at an instant.

Stimulation parameter selector 842 selects the approximately optimal value for the stimulation parameter from the plurality of parameter values. HRV measurement circuit 220 produces the HRV parameter for the stimulation

parameter optimization period. Each value produced and tested for the stimulation parameter is associated with one or more values of the HRV parameter. Stimulation parameter selector 842 selects the approximately optimal value for the stimulation parameter as the value corresponding to a maximum value of the HRV parameter produced for the stimulation parameter optimization period.

In one exemplary specific embodiment, physiologic parameter measurement module 844 includes an atrioventricular interval (AVI) measurement module to measure an AVI as an intrinsic time interval between an atrial depolarization and a successive ventricular depolarization. Stimulation parameter generator 838 produce a plurality of values of an AVD based on the AVI. Pulse output controller 840 includes a pacing output controller to control the delivery of a plurality of series of pacing pulses, with each value produced for the AVD being used for one or more series of the plurality of series of pacing pulses. Stimulation parameter selector 842 includes a pacing parameter selector that selects an approximately optimal value from the plurality of values produced for the AVD. The approximately optimal value is the value corresponding to a maximum value of the HRV parameter produced for the stimulation parameter optimization period.

When two or more stimulation parameters are to be optimized, stimulation parameter generator 838 produces a plurality of values for each stimulation parameter. Pulse output controller 840 controls the delivery of a plurality of series of stimulation pulses. Each series of stimulation pulses is delivered using a combination of values produced for all the stimulation parameters to be optimized. Stimulation parameter selector 842 selects an approximately optimal combination of values for all the stimulation parameters to be optimized. The approximately optimal combination of values is the combination of values corresponding to a maximum value of the HRV parameter produced for the stimulation parameter optimization period.

FIG. 9 is a block diagram illustrating another embodiment of a stimulation parameter optimization module 931, which is another embodiment of stimulation parameter optimization module 731. Stimulation parameter optimization module 931 includes an optimization timer 946, a stimulation parameter generator 938, a pulse output controller 940, and a stimulation

parameter selector 942. Stimulation parameter optimization module 931 determines and selects an approximately optimal value for at least one dynamic stimulation parameter by delivering stimulation pulses using dynamically produced values for the dynamic stimulation parameter while measuring the HRV. The dynamically produced values of the dynamic stimulation parameter are evaluated by their effect on an HRV parameter. As one embodiment of stimulation parameter optimization module 731, stimulation parameter optimization module 931 is applicable for optimization of pacing parameters, neurostimulation parameters, or both.

Optimization timer 946 starts the stimulation parameter optimization period during which the values for the dynamic stimulation parameter are dynamically produced and evaluated and the approximately optimal value for the stimulation parameter is determined. In one embodiment, optimization timer 946 starts the stimulation parameter optimization period according to a predetermined schedule, such as on a periodic basis. In another embodiment, optimization timer 946 starts the stimulation parameter optimization period as requested by a person such as a physician, other caregiver, or the patient. Optimization timer 946 stops the stimulation parameter optimization period after a predetermined period of time. The approximately optimal value for the stimulation parameter is selected at the end of the stimulation parameter optimization period. In one embodiment, the stimulation parameter optimization period covers a period in which a wide variety of activities are anticipated for the patient, such as a period of 24 hours.

Stimulation parameter generator 938 dynamically produces the values for the dynamic stimulation parameter. In one embodiment, as illustrated in FIG. 9, stimulation parameter generator 938 includes a physiologic parameter measurement module 944 and a dynamic stimulation parameter generator 948. Physiologic parameter measurement module 944 measures at least one physiologic parameter related to the patient's cardiac condition. Dynamic stimulation parameter generator 948 dynamically produce values of the dynamic stimulation parameter based on the physiologic parameter.

Pulse output controller 940 controls the delivery of stimulation pulses using the dynamically produced values of the dynamic stimulation parameter. Pulse output controller 940 includes a stimulation algorithm execution module to

control the delivery of stimulation pulses by executing a stimulation algorithm using the dynamic stimulation parameter whose value is updated each time when the dynamically produced value differs from the value being used. In various embodiments, the stimulation algorithm execution module includes one or more of a bradycardia pacing algorithm execution module, a CRT pacing algorithm execution module, an RCT pacing algorithm execution module, an autonomic neurostimulation algorithm execution module, and a combined pacing-neurostimulation algorithm execution module. One of such algorithm execution modules is activated at an instant.

Stimulation parameter selector 942 selects the approximately optimal value for the stimulation parameter from the dynamically produced values. HRV measurement circuit 220 produces the HRV parameter for the stimulation parameter optimization period. Each dynamically produced value for the stimulation parameter is associated with one or more values of the HRV parameter. Stimulation parameter selector 942 selects the approximately optimal value for the stimulation parameter as the value corresponding to a maximum value of the HRV parameter produced for the stimulation parameter optimization period.

In one exemplary specific embodiment, physiologic parameter measurement module 944 includes a heart rate monitor that monitors the patient's heart rate during the stimulation parameter optimization period. Dynamic stimulation parameter generator 948 includes a dynamic AVD generator to dynamically produce values of a dynamic AVD as a function of the heart rate. Pulse output controller 940 includes a pacing output controller to control the delivery of pacing pulses using the dynamic AVD during the stimulation parameter optimization period. Stimulation parameter selector 942 includes a pacing parameter selector that selects an approximately optimal AVD value being the value of the dynamic AVD corresponding to a maximum value of the HRV parameter produced for the stimulation parameter optimization period.

When two or more dynamic stimulation parameters are to be optimized, stimulation parameter generator 938 dynamically produces values for all these dynamic stimulation parameters. Pulse output controller 940 controls the delivery of stimulation pulses using a combination of the dynamically produced

values for all the dynamic stimulation parameters. Each unique combination of the dynamically produced values for the stimulation parameter is associated with one or more values of the HRV parameter. Stimulation parameter selector 942 selects an approximately optimal combination of values for the stimulation parameters as the unique combination that corresponds to a maximum value of the HRV parameter produced for the stimulation parameter optimization period.

FIG. 10 is a flow chart illustrating one embodiment of a method for stimulation parameter optimization using an HRV parameter. In one embodiment, the method is performed by stimulation system 715.

A stimulation parameter optimization period is started at 1000. This starts the process of optimizing at least one stimulation parameter as illustrated in FIG. 10. The stimulation parameter optimization period lasts until the process is completed. The stimulation parameter includes, but not limited to, an AVD, an IVD, pacing sites, neurostimulation pulse frequency, and neurostimulation sites.

A signal indicative of a cardiac function is sensed at 1010. The signal includes one or more of an atrial electrogram, a ventricular electrogram, a neural signal indicative of sympathetic neural activities, and a signal indicative of parasympathetic neural activities. At least one cardiac signal allowing for measurement of an HRV parameter is sensed.

A plurality of parameter values for the stimulation parameter is produced at 1020. In one embodiment, a physiologic parameter related to a patient's cardiac condition is measured at the beginning of the stimulation parameter optimization period. The plurality of parameter values are calculated based on the physiological parameter. In another embodiment, a physiologic parameter related to a patient's cardiac condition is monitored throughout the stimulation parameter optimization period. The value for the stimulation parameter is dynamically calculated as a function of the physiological parameter, which changes dynamically during the stimulation parameter optimization period.

Electrical stimulation pulses are delivered using the plurality of parameter values at 1030. In one embodiment, pacing pulses are delivered. In another embodiment, neurostimulation pulses are delivered. In another embodiment, pacing and neurostimulation pulses are delivered in a temporally coordinated manner. The electrical stimulation pulses are delivered by executing

a stimulation algorithm during the stimulation parameter optimization period. The stimulating algorithm uses the stimulation parameter that is to be optimized. Examples of the stimulation algorithm include, but are not limited to a bradycardia pacing algorithm, a CRT pacing algorithm, an RCT pacing algorithm, an autonomic neurostimulation algorithm, and a combined pacing-neurostimulation algorithm.

The HRV is measured based on the sensed cardiac signal, and at least one HRV parameter is produced based on the HRV measurement, at 1040. In one embodiment, the sensed cardiac signal is an atrial electrogram, and the HRV parameter is produced based on atrial intervals measured from the atrial electrogram. In another embodiment, the sensed cardiac signal is a ventricular electrogram, and the HRV parameter is produced based on ventricular intervals measured from the ventricular electrogram.

An approximately optimal parameter value for the stimulation parameter is selected from the plurality of parameter values produced during the stimulation parameter optimization period at 1050. The approximately optimal parameter value corresponding to a maximum value of the HRV parameter produced for the stimulation parameter optimization period.

EXAMPLE 3: HRV-Driven Therapy On/Off Switch

The benefit of an electrical stimulation therapy may depend on a patient's cardiac condition and physical activity level, both changing over time. To maximize the benefit to the patient, the therapy need to be adaptive to the patient's condition and needs. Some patients receive two or more therapies cannot or should not be administered simultaneously. The HRV provides for a signal triggering the start, stop, and/or adjustment of therapies. In one embodiment, an HRV parameter is used as a safety check on the delivery of a therapy. The delivery of the therapy is suspended when the HRV parameter indicates that continued delivery of the therapy is potentially harmful to the patient. In another embodiment, an HRV parameter is monitored as a signal indicative of a need to switch from one therapy to another in response to a change in the patient's condition.

For example, a patient having suffered MI has a decreased hemodynamic performance and goes through an adverse cardiac remodeling process. In one

embodiment, a CRT is delivered to improve the post MI patient's hemodynamic performance, and an RCT is delivered to reduce the post MI remodeling. Generally, the CRT and RCT cannot be delivered simultaneously because of conflicts between their effects. The RCT treats post MI patients by controlling the progress of post MI remodeling by reducing the preload in the infarct region. Pacing pulses are delivered with a short AVD to reduce the stress to this region prior to contraction. However, pacing with the short AVD may result in reduced hemodynamic performance. For example, if the heart being paced with the short AVD has a normal ventricular conduction (Purkinje) system, the pacing lowers the degree of ventricular synchrony and the cardiac output, which are measures of hemodynamic performance. One consequent problem is that when a post MI patient becomes active, the pacing with the short AVD may limit the cardiac output and hence, prevent the heart from pumping sufficient blood to meet the patient's metabolic need. One solution is to deliver the CRT and RCT on an alternating basis, depending on the instantaneous metabolic need of the post MI patient, such that the pacing provides for optimal hemodynamic performance when the metabolic need is high, and post MI remodeling control when the metabolic need is low. In one embodiment, an HRV parameter is used to control the timing for switching between the CRT and RCT. In one specific embodiment, when the HRV parameter falls below a threshold, the patient stops receiving the RCT and starts to receive the CRT. In one specific embodiment, the HRV parameter is used in combination with another one or more parameters, such as a physical activity level parameter, to control the timing for switching between the CRT and RCT. In another embodiment, an RV bradycardia pacing is delivered to improve the post-MI patient's hemodynamic performance, and the RCT is delivered to reduce the degree of post MI remodeling. The HRV parameter is used to control the timing for switching between the RV bradycardia pacing and RCT in substantially the same manner as discussed above, with the CRT being replaced with the RV bradycardia pacing.

FIG. 11 is a block diagram illustrating one embodiment of a stimulation system 1115 with an HRV-driven therapy switch system. Stimulation system 1115 is a specific embodiment of stimulation system 115 and includes sensing circuit 212, pulse output circuit 214, HRV measurement circuit 220, and a stimulation control circuit 1130.

Stimulation control circuit 1130 includes a stimulation algorithm execution module 1150 and a safety check module 1152. Stimulation algorithm execution module 1150 controls the delivery of the electrical stimulation pulses by executing at least one stimulation algorithm. As a specific embodiment of stimulation system 115, stimulation system 1115 includes one or both of a pacing system and a neurostimulation system. Stimulation algorithm execution module 1150 includes one or more of a bradycardia pacing algorithm execution module, a CRT pacing algorithm execution module, an RCT pacing algorithm execution module, a neurostimulation algorithm execution module, and a combined pacing-neurostimulation algorithm execution module. One of such algorithm execution module is activated at an instant.

Safety check module 1152 stops the execution of the stimulation algorithm based on the HRV parameter produced by HRV measurement circuit 220. In one embodiment, as illustrated in FIG. 11, safety check module 1152 includes a comparator 1154 and a switch circuit 1156. Comparator 1154 receives the HRV parameter from HRV measurement circuit 220 and compares the HRV parameter to a safety threshold. Switch circuit 1156 stops the execution of the stimulation algorithm when the HRV parameter falls below the safety threshold. In a further embodiment, switch circuit 1156 resumes the execution of the stimulation algorithm when the HRV parameter exceeds another safety threshold. The values of the two safety thresholds are determined based on specific considerations in cardiac condition management and can be equal or different. In one exemplary specific embodiment, the stimulation algorithm is the RCT pacing algorithm. Safety check module 1152 stops the executing of the RCT pacing algorithm when the patient's HRV indicates or suggests a worsening hemodynamic performance. In another exemplary specific embodiment, the stimulation algorithm is the bradycardia pacing algorithm. Safety check module 1152 stops the executing of the bradycardia pacing algorithm when the patient's HRV indicates or suggests that the pacing negatively affects the patient's cardiac condition.

In another embodiment, switch circuit 1156 stops the execution of a first stimulation algorithm and starts the execution of a second stimulation algorithm when the HRV parameter falls below a first safety threshold, and stops the execution of the second stimulation algorithm and starts the execution of the first

stimulation algorithm when the HRV parameter exceeds a second safety threshold. Depending on specific cardiac condition management considerations, the first safety threshold can be higher than, equal to, or lower than the second safety threshold. In one exemplary specific embodiment, the first stimulation algorithm is the RCT pacing algorithm, and the second stimulation algorithm is the CRT pacing algorithm. In another exemplary specific embodiment, the first stimulation algorithm is the RCT pacing algorithm, and the second stimulation algorithm is the bradycardia pacing algorithm.

In one embodiment, safety check module 1152 includes a safety threshold generator to dynamically adjust the safety threshold(s) based on an indication, estimation, or prediction of the patient's activity level. In one specific embodiment, the safety threshold generator adjusts one or more safety thresholds based on the patient's heart rate. In another embodiment, the safety threshold generator adjusts one or more safety thresholds based the patient's anticipated activity level during specific times of each day.

FIG. 12 is a flow chart illustrating one embodiment of a method for starting and stopping a therapy using an HRV parameter. In one embodiment, the method is performed by stimulation system 1115.

A signal indicative of a cardiac function is sensed at 1200. The signal includes one or more of an atrial electrogram, a ventricular electrogram, a neural signal indicative of sympathetic neural activities, and a signal indicative of parasympathetic neural activities. At least one cardiac signal allowing for measurement of an HRV parameter is sensed.

The HRV is measured based on the sensed cardiac signal, and at least one HRV parameter is produced based on the HRV measurement, at 1210. In one embodiment, the sensed cardiac signal is an atrial electrogram, and the HRV parameter is produced based on atrial intervals measured from the atrial electrogram. In another embodiment, the sensed cardiac signal is a ventricular electrogram, and the HRV parameter is produced based on ventricular intervals measured from the ventricular electrogram.

Electrical stimulation pulses are delivered by executing a stimulation algorithm at 1220. Examples of the stimulation algorithm includes a bradycardia pacing algorithm, a CRT pacing algorithm, an RCT pacing algorithm, a neurostimulation algorithm, and a combined pacing-neurostimulation algorithm.

The execution of the stimulation algorithm is stopped when the HRV parameter is out of a safety window at 1230. In one embodiment, the HRV parameter is compared to a safety threshold. The execution of the first stimulation algorithm is stopped when the HRV parameter falls below the safety threshold. In a further embodiment, the execution of the stimulation algorithm is resumed when the HRV parameter exceeds another safety threshold. In another embodiment, the execution of a first stimulation algorithm is stopped, and the execution of a second stimulation algorithm is started, when the HRV parameter falls below a first safety threshold. The execution of the first stimulation algorithm is started, and the execution of the second stimulation algorithm is stopped, when the HRV parameter exceeds a second safety threshold.

In one embodiment, the safety window is dynamically adjusted based on an indication, estimation, or prediction of the patient's activity level. In one specific embodiment, the safety window is adjusted based on the patient's heart rate. In another embodiment, the safety window is adjusted based the patient's anticipated activity level during specific times of each day.

It is to be understood that the above detailed description, including Examples 1 – 3, is intended to be illustrative, and not restrictive. Other embodiments, including any possible permutation of the system components discussed in this document, will be apparent to those of skill in the art upon reading and understanding the above description. The scope of the invention should, therefore, be determined with reference to the appended claims, along with the full scope of equivalents to which such claims are entitled.

What is claimed is:

1. A cardiac rhythm management system comprising:

a pulse output circuit to deliver electrical stimulation pulses;

a sensing circuit to sense a cardiac signal;

a heart rate variability (HRV) measurement circuit, coupled to the sensing circuit, to measure an HRV being a variance in cardiac cycle lengths over a predetermined period of time based on the sensed cardiac signal and to produce an HRV parameter based on the HRV measurement; and

a stimulation control circuit, coupled to the pulse output circuit, the sensing circuit, and the HRV measurement circuit, the stimulation control circuit including a stimulation parameter optimization module adapted to adjust at least one stimulation parameter to an approximately optimal value based on the HRV parameter, the stimulation parameter optimization module including:

a stimulation parameter generator adapted to produce a plurality of parameter values for the at least one stimulation parameter;

a pulse output controller adapted to control the delivery of the electrical stimulation pulses using the plurality of parameter values during a stimulation parameter optimization period; and

a stimulation parameter selector adapted to select the approximately optimal value for the at least one stimulation parameter from the plurality of parameter values, the approximately optimal parameter value corresponding to a maximum value of the HRV parameter measured for the stimulation parameter optimization period.

2. The system according to claim 1, wherein the stimulation parameter optimization module comprises an optimization timer to start the stimulation parameter optimization period.

3. The system according to claim 2, wherein the optimization timer is programmed to start the stimulation parameter optimization period on a periodic basis.

4. The system according to any of claims 2 and 3, wherein the optimization timer is further adapted to stop the stimulation parameter optimization period.

5. The system according to any of the preceding claims, wherein the stimulation parameter generator comprises a physiologic parameter measurement module adapted to measure at least one physiologic parameter, and wherein the stimulation parameter generator is adapted to produce the plurality of parameter values for the at least one stimulation parameter based on the at least one physiologic parameter, and wherein the pulse output controller is adapted to control the delivery of the plurality of electrical stimulation pulse series each including a plurality of electrical stimulation pulses to be delivered using one parameter value of the plurality of parameter values during the stimulation parameter optimization period.

6. The system according to any of claims 1 to 4, wherein the stimulation parameter generator comprises a physiologic parameter measurement module to measure at least one physiologic parameter and a dynamic stimulation parameter generator to dynamically produce parameter values of at least one dynamic stimulation parameter based on the at least one physiologic parameter, the pulse output controller is adapted to control the delivery of electrical stimulation pulses using the dynamically produced parameter values of the at least one dynamic stimulation parameter, and the stimulation parameter selector is adapted to identify an approximately optimal value being a value of the dynamic stimulation parameter corresponding to a maximum value of the HRV parameter measured for the stimulation parameter optimization period.

7. The system according to any of the preceding claims, wherein the pulse output controller comprises a stimulation algorithm execution module to control the delivery of the electrical stimulation pulses by executing a stimulation algorithm during the stimulation parameter optimization period.

8. The system according to claim 7, wherein the stimulation algorithm execution module comprise a bradycardia pacing algorithm execution module.

9. The system according to any of claims 7 and 8, wherein the stimulation algorithm execution module comprises a cardiac resynchronization therapy (CRT) pacing algorithm execution module.

10. The system according to any of claims 7 to 9, wherein the stimulation algorithm execution module comprises a remodeling control therapy (RCT) pacing algorithm execution module.

11. The system according to any of claims 7 to 10, wherein the stimulation algorithm execution module comprises an autonomic neurostimulation algorithm execution module.

12. The system according to claim 7, wherein the stimulation algorithm execution module comprise a combined pacing and neurostimulation algorithm execution module.

13. The system according to any of the preceding claims, wherein the pulse output circuit comprises a pacing output circuit to deliver cardiac pacing pulses, and the stimulation control circuit comprises a pacing control circuit including a pacing parameter optimization module to adjust at least one pacing parameter to an approximately optimal value based on the HRV parameter.

14. The system according to claim 13, wherein the pacing parameter optimization module comprises an atrioventricular delay (AVD) optimization module adapted to optimize one or more AVDs.

15. The system according to any of claims 13 and 14, wherein the pacing parameter optimization module comprises an interventricular delay (IVD) optimization module adapted to optimize one or more IVDs.

16. The system according to any of claims 13 to 15, wherein the pacing parameter optimization module comprises a pacing site optimization module adapted to optimize a selection of one or more sites to which the cardiac pacing pulses are delivered.

17. The system according to any of the preceding claims, wherein the pulse output circuit comprises a neurostimulation circuit to deliver neurostimulation pulses, and the stimulation control circuit comprises a neurostimulation control circuit including a neurostimulation parameter optimization module to adjust at least one neurostimulation parameter to an approximately optimal value based on the HRV parameter.

18. The system according to claim 17, wherein the neurostimulation parameter optimization module comprises a stimulation pulse frequency optimization module adapted to optimize one or more stimulation pulse frequencies.

19. The system according to any of claims 17 and 18, wherein the neurostimulation parameter optimization module comprises a stimulation site optimization module adapted to optimize a selection of one or more sites to which the neurostimulation pulses are delivered.

20. The system according to any of the preceding claims, wherein the HRV measurement circuit comprises one or more of a Standard Deviation of Normal-to-Normal intervals (SDNN) generator to produce an SDNN, a Standard Deviation of Averages of Normal-to-Normal intervals (SDANN) generator to produce an SDANN, a Ratio of Low Frequency HRV to High Frequency HRV ratio (LF/HF ratio) generator to produce an LF/HF ratio, an HRV footprint generator to produce an HRV footprint, and a Root-Mean-Square of Successive Differences (RMSSD) generator to produce an RMSSD.

21. The system according to any of claims 1 to 19, wherein the HRV measurement circuit comprises an autonomic balance monitor to monitor a parameter indicative of a balance between sympathetic and parasympathetic activities.

22. The system according to claim 21, wherein the autonomic balance monitor comprises a Ratio of Low Frequency HRV to High Frequency HRV ratio (LF/HF ratio) generator to produce an LF/HF ratio.

23. A method comprising:

starting a stimulation parameter optimization period;

sensing a cardiac signal;

producing a plurality of parameter values for at least one stimulation parameter;

delivering electrical stimulation pulses using the plurality of parameter values for the at least one stimulation parameter during the stimulation parameter optimization period;

measuring a variance in cardiac cycle lengths over a predetermined period of time to produce at least one heart rate variability (HRV) parameter based on the cardiac signal sensed during the stimulation parameter optimization period;

selecting an approximately optimal value for the at least one stimulation parameter from the plurality of parameter values, the approximately optimal value corresponding to a maximum value of the HRV parameter measured during the stimulation parameter optimization period.

24. The method according to claim 23, wherein starting the stimulation parameter optimization period comprises starting the stimulation parameter optimization period on a periodic basis.

25. The method according to any of claims 23 and 24, further comprising programming the stimulation parameter optimization period for a period associated with low physical activity level.

26. The method according to any of claims 23 to 25, further comprising measuring a physiologic parameter, and wherein producing the plurality of parameter values for the at least one stimulation parameter comprises producing the plurality of parameter values for the at least one stimulation parameter based on the measured physiologic parameter, and delivering the electrical stimulation pulses comprises delivering a plurality of stimulation pulse series each including a plurality of stimulation pulses to be delivered using one parameter value of the plurality of parameter values during the stimulation parameter optimization period.

27. The method according to any of claims 23 to 25, further comprising measuring a dynamically changing physiologic parameter, and wherein producing the plurality of parameter values comprises dynamically producing values of a dynamic stimulation parameter based on the dynamically changing physiologic parameter during the stimulation parameter optimization period, delivering the electrical stimulation pulses comprises delivering stimulation pulses using the values of the dynamic stimulation parameter during the stimulation parameter optimization period, and selecting the approximately optimal value for the at least one stimulation parameter including comprises selecting the approximately optimal value from the values of the dynamic stimulation parameter produced during the stimulation parameter optimization period, the approximately optimal value corresponding to a maximum value of the HRV parameter measured for the stimulation parameter optimization period.

28. The method according to any of claims 23 to 27, wherein delivering electrical stimulation pulses comprises delivering pacing pulses.

29. The method according to claim 28, wherein delivering pacing pulses comprises delivering the pacing pulses by executing a pacing algorithm during the stimulation parameter optimization period, the pacing algorithm using the at least one stimulation parameter.

30. The method according to claim 29, wherein executing the pacing algorithm comprises executing at least one of a bradycardia pacing algorithm, a cardiac resynchronization therapy (CRT) pacing algorithm and a remodeling control therapy (RCT) pacing algorithm.

31. The method according to any of claims 28 to 30, wherein the at least one stimulation parameter comprises an atrioventricular delay (AVD).

32. The method according to any of claims 28 to 31, wherein the at least one stimulation parameter comprises an interventricular delay (IVD).

33. The method according to any of claims 28 to 32, wherein the at least one stimulation parameter comprises a pacing site parameter identifying sites to which the pacing pulses are delivered.

34. The method according to any of claims 23 to 33, wherein delivering the electrical stimulation pulses comprises delivering neurostimulation pulses.

35. The method according to claim 34, wherein delivering neurostimulation pulses comprises delivering the neurostimulation pulses by executing a neurostimulation algorithm during the stimulation parameter optimization period, the neurostimulation algorithm using the at least one stimulation parameter.

36. The method according to any of claims 34 and 35, wherein the at least one stimulation parameter comprises a stimulation frequency.

37. The method according to any of claims 34 to 36, wherein the at least one stimulation parameter comprises a stimulation site parameter identifying sites to which the neurostimulation pulses are delivered.

38. The method according to any of claims 23 to 37, wherein measuring HRV to produce the HRV parameter comprises measuring HRV to produce one or more of a Standard Deviation of Normal-to-Normal intervals (SDNN), a Standard Deviation of Averages of Normal-to-Normal intervals (SDANN), a Ratio of Low Frequency HRV to High Frequency HRV ratio (LF/HF ratio), an HRV footprint, and a Root-Mean-Square of Successive Differences (RMSSD).

39. The method according to any of claims 23 to 37, wherein measuring HRV to produce the HRV parameter comprises measuring HRV to produce a parameter indicative of a balance between sympathetic and parasympathetic activities.

40. The method according to claim 39, wherein measuring HRV to produce the parameter indicative of the balance between sympathetic and parasympathetic activities comprises producing a Ratio of Low Frequency HRV to High Frequency HRV ratio (LF/HF ratio).

41. A cardiac rhythm management system, comprising:

a pacing output circuit to deliver pacing pulses;

a sensing circuit to sense a cardiac signal;

a heart rate variability (HRV) measurement circuit, coupled to the sensing circuit, to measure an HRV being a variance in cardiac cycle lengths over a predetermined period of time based on the sensed cardiac signal and to produce an HRV parameter based on the HRV measurement; and

a pacing control circuit coupled to the pacing output circuit, the sensing circuit, and the HRV measurement circuit, the pacing control circuit including:

a pacing algorithm execution module to control the delivery of the pacing pulses by executing an atrial tracking pacing algorithm using pacing parameters including a maximum tracking rate (MTR); and

an MTR adjustment module coupled to the HRV measurement circuit and the pacing algorithm execution module, the MTR adjustment circuit adapted to adjust the MTR based on the HRV parameter.

42. The system according to claim 41, wherein the cardiac signal comprises an electrogram.

43. The system according to any of claims 41 and 42, wherein the pacing algorithm execution module comprises a bradycardia pacing algorithm execution module.

44. The system according to any of claims 41 to 43, wherein the pacing algorithm execution module comprises a cardiac resynchronization therapy (CRT) pacing algorithm execution module.

45. The system according to any of claims 41 to 44, wherein the pacing algorithm execution module comprises a remodeling control therapy (RCT) pacing algorithm execution module.

46. The system according to any of claims 41 to 45, wherein the MTR adjustment module comprises an MTR selector adapted to select a value for the MTR from a plurality of predetermined values based on the HRV parameter.

47. The system according to claim 46, wherein the MTR selector comprises a comparator to compare the HRV parameter to a threshold HRV level, and wherein the MTR selector is adapted to set the MTR to a predetermined first value if the HRV parameter exceeds the predetermined threshold and a predetermined second value if the HRV parameter does not exceed the threshold HRV level.

48. The system according to claim 47, wherein the MTR adjustment module further comprises an HRV threshold generator to dynamically adjust the threshold HRV level based on an activity level.

49. The system according to any of claims 41 to 48, wherein the HRV measurement circuit comprises one or more of a Standard Deviation of Normal-to-Normal intervals (SDNN) generator to produce an SDNN, a Standard Deviation of Averages of Normal-to-Normal intervals (SDANN) generator to produce an SDANN, a Ratio of Low Frequency HRV to High Frequency HRV ratio (LF/HF ratio) generator to produce an LF/HF ratio, an HRV footprint generator to produce an HRV footprint, and a Root-Mean-Square of Successive Differences (RMSSD) generator to produce an RMSSD.

50. The system according to any of claims 41 to 48, wherein the HRV measurement circuit comprises an autonomic balance monitor to monitor a parameter indicative of a balance between sympathetic and parasympathetic activities.

51. The system according to claim 50, wherein the autonomic balance monitor comprises a Ratio of Low Frequency HRV to High Frequency HRV ratio (LF/HF ratio) generator to produce an LF/HF ratio.

52. A method for operating a cardiac pacemaker, comprising:

sensing a cardiac signal;

measuring a variance in cardiac cycle lengths over a predetermined period of time to produce a heart rate variability (HRV) parameter based on the sensed cardiac signal;

executing an atrial tracking pacing algorithm to control pacing pulse deliveries, the atrial tracking pacing algorithm using pacing parameters including a maximum tracking rate (MTR); and

adjusting the MTR based on the HRV parameter.

53. The method according to claim 52, wherein sensing a cardiac signal comprises sensing an electrogram.

54. The method according to any of claims 52 and 53, wherein executing the atrial tracking pacing algorithm comprises executing one of a bradycardia pacing algorithm, a CRT pacing algorithm, and a post-MI RCT pacing algorithm.

55. The method according to any of claims 52 to 54, wherein adjusting the MTR based on the HRV parameter comprising setting the MTR to one of a plurality of predetermined values based on the HRV parameter.

56. The method according to claim 55, wherein setting the MTR to one of the plurality of predetermined values based on the HRV parameter comprises:

comparing the HRV parameter to a threshold HRV level; and

setting the MTR to a first value if the HRV parameter exceeds the threshold HRV level and a second value if the HRV parameter does not exceed the threshold HRV level.

57. The method according to claim 56, further comprising dynamically adjusting the threshold HRV level based on a heart rate.

58. The method according to any of claims 56 and 57, further comprising dynamically adjusting the threshold HRV level based on an indication, estimation, or prediction of an activity level.

59. The method according to any of claims 52 to 58, wherein measuring HRV to produce the HRV parameter comprises measuring HRV to produce one or more of a Standard Deviation of Normal-to-Normal intervals (SDNN), a Standard Deviation of Averages of Normal-to-Normal intervals (SDANN), a Ratio of Low Frequency HRV to High Frequency HRV ratio (LF/HF ratio), an HRV footprint, and a Root-Mean-Square of Successive Differences (RMSSD).

60. The method according to any of claims 52 to 58, wherein measuring HRV to produce the HRV parameter comprises measuring HRV to produce a parameter indicative of a balance between sympathetic and parasympathetic activities.

61. The method according to claim 60, wherein measuring HRV to produce the parameter indicative of the balance between sympathetic and parasympathetic activities comprises producing a Ratio of Low Frequency HRV to High Frequency HRV ratio (LF/HF ratio).

62. A cardiac rhythm management system, comprising:

a sensing circuit to sense a cardiac signal;

a heart rate variability (HRV) measurement circuit, coupled to the sensing circuit, to measure an HRV being a variance in cardiac cycle lengths over a predetermined period of time based on the sensed cardiac signal and to produce an HRV parameter based on the HRV measurement;

a pulse output circuit to deliver electrical stimulation pulses; and

a stimulation control circuit coupled to the sensing circuit, the HRV measurement circuit, and the pulse output circuit, the stimulation control circuit including:

a stimulation algorithm execution module to control the delivery of the electrical stimulation pulses by executing at least a first stimulation algorithm; and

a safety check module to stop the execution of the first stimulation algorithm based on the HRV parameter.

63. The system according to claim 62, wherein the sensing circuit comprises an electrogram sensing circuit to sense one or more electrograms, and the pulse output circuit comprises a pacing output circuit to deliver pacing pulses.

64. The system according to claim 63, wherein the stimulation algorithm execution module comprises a bradycardia pacing algorithm execution module to control the delivery of the pacing pulses by executing a bradycardia pacing algorithm.

65. The system according to any of claims 63 and 64, wherein the stimulation algorithm execution module comprises a cardiac resynchronization therapy (CRT) pacing algorithm execution module to control the delivery of the pacing pulses by executing a CRT pacing algorithm.

66. The system according to any of claims 63 to 65, wherein the stimulation algorithm execution module comprises a remodeling control therapy (RCT) pacing algorithm execution module to control the delivery of the pacing pulses by executing an RCT pacing algorithm.

67. The system according to any of claims 62 to 66, wherein the sensing circuit comprises a neural signal sensing circuit to sense one or more autonomic neural signals, and the pulse output circuit comprises a neurostimulation output circuit to deliver neurostimulation pulses.

68. The system according to claim 67, wherein the stimulation algorithm execution module comprises a neurostimulation algorithm execution module to control the delivery of the neurostimulation pulses by executing a first neurostimulation algorithm.

69. The system according to any of claims 62 to 68, wherein the safety check module comprises:

a comparator to compare the HRV parameter to a first safety threshold; and

a switch circuit adapted to stop the execution of the first stimulation algorithm when the HRV parameter falls below the first safety threshold.

70. The system according to claim 69, wherein the safety check module further comprises a safety threshold generator to dynamically adjust the first safety threshold based on an activity level.

71. The system according to claim 69, wherein the comparator is adapted to compare the HRV parameter to the first safety threshold and a second safety threshold, and the switch circuit is adapted to resume the execution of the first stimulation algorithm when the HRV parameter exceeds the second safety threshold.

72. The system according to claim 71, wherein the switch circuit is adapted to stop the execution of the first stimulation algorithm and to start an execution of a second stimulation algorithm when the HRV parameter falls below the first safety threshold.

73. The system according to claim 72, wherein the comparator is adapted to compare the HRV parameter to the first safety threshold and a second safety threshold, and the switch circuit is adapted to stop the execution of the second stimulation algorithm and to start the execution of the first stimulation algorithm when the HRV parameter exceeds the second safety threshold.

74. The system according to any of claims 62 to 73, wherein the HRV measurement circuit comprises one or more of a Standard Deviation of Normal-to-Normal intervals (SDNN) generator to produce an SDNN, a Standard Deviation of Averages of Normal-to-Normal intervals (SDANN) generator to produce an SDANN, a Ratio of Low Frequency HRV to High Frequency HRV ratio (LF/HF ratio) generator to produce an LF/HF ratio, an HRV footprint

generator to produce an HRV footprint, and a Root-Mean-Square of Successive Differences (RMSSD) generator to produce an RMSSD.

75. The system according to any of claims 62 to 73, wherein the HRV measurement circuit comprises an autonomic balance monitor to monitor a parameter indicative of a balance between sympathetic and parasympathetic activities.

76. The system according to claim 75, wherein the autonomic balance monitor comprises a Ratio of Low Frequency HRV to High Frequency HRV ratio (LF/HF ratio) generator to produce an LF/HF ratio.

77. A method, comprising:

sensing a cardiac signal;

measuring a variance in cardiac cycle lengths over a predetermined period of time to produce an HRV parameter based on the sensed cardiac signal;

delivering electrical stimulation pulses by executing at least a first stimulation algorithm; and

stopping the execution of the first stimulation algorithm when the HRV parameter is out of a safety window.

78. The method according to claim 77, wherein sensing the cardiac signal comprises sensing one or more one electrograms, and delivering the electrical stimulation pulses comprises delivering pacing pulses.

79. The method according to any of claims 77 and 78, further comprising sensing one or more neural signals, and delivering the electrical stimulation pulses comprises delivering neurostimulation pulses.

80. The method according to any of claims 77 to 79, further comprising dynamically adjusting the safety window based on a heart rate.

81. The method according to any of claims 77 to 80, further comprising dynamically adjusting the safety window based on an indication, estimation, or prediction of an activity level.

82. The method according to any of claims 77 to 81, wherein stopping the execution of the first stimulation algorithm when the HRV parameter is out of the safety window comprises:

comparing the HRV parameter to a first safety threshold; and

stopping the execution of the first stimulation algorithm when the HRV parameter falls below the first safety threshold.

83. The method according to any of claims 77 to 82, wherein the first stimulation algorithm comprises a bradycardia pacing algorithm.

84. The method according to any of claims 77 to 83, wherein the first stimulation algorithm comprises a remodeling control therapy (RCT) pacing algorithm.

85. The method according to claim 82, further comprising:

comparing the HRV parameter to a second safety threshold; and

resuming the execution of the first stimulation algorithm when the HRV parameter exceeds the second safety threshold.

86. The method according to claim 85, further comprising starting an execution of a second stimulation algorithm when the HRV parameter falls below the first safety threshold.

87. The method according to claim 86, further comprising stopping the execution of the second stimulation algorithm when the HRV parameter exceeds the second safety threshold.

88. The method according to claim 87, wherein the first stimulation algorithm is a remodeling control (RCT) pacing algorithm, and the second stimulation algorithm is a cardiac resynchronization (CRT) pacing algorithm.

89. The method according to claim 87, wherein the first stimulation algorithm is a remodeling control (RCT) pacing algorithm, and the second stimulation algorithm is a bradycardia pacing algorithm.

90. The method according to claim 87, wherein the first stimulation algorithm is a parasympathetic nerve stimulation algorithm, and the second therapy is a sympathetic nerve stimulation algorithm.

91. The method according to any of claims 77 to 90, wherein measuring HRV to produce the HRV parameter comprises measuring HRV to produce one or more of a Standard Deviation of Normal-to-Normal intervals (SDNN), a Standard Deviation of Averages of Normal-to-Normal intervals (SDANN), a Ratio of Low Frequency HRV to High Frequency HRV ratio (LF/HF ratio), an HRV footprint, and a Root-Mean-Square of Successive Differences (RMSSD).

92. The method according to any of claims 77 to 90, wherein measuring HRV to produce the HRV parameter comprises measuring HRV to produce a parameter indicative of a balance between sympathetic and parasympathetic activities.

93. The method according to claim 92, wherein measuring HRV to produce the parameter indicative of the balance between sympathetic and parasympathetic activities comprises producing a Ratio of Low Frequency HRV to High Frequency HRV ratio (LF/HF ratio).

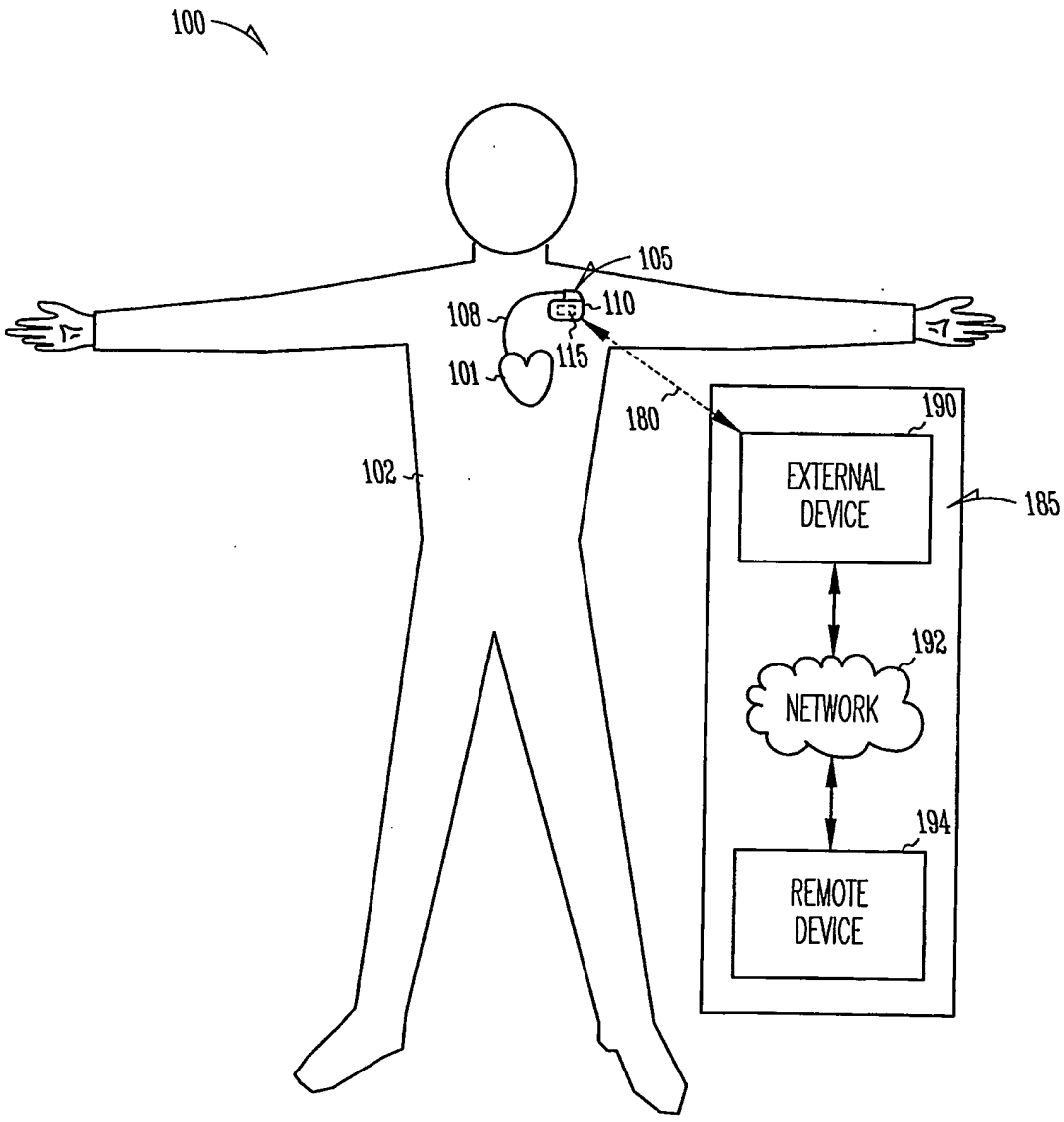
100
105
108
110
115
101
180
190
EXTERNAL DEVICE
185
102
192
NETWORK
194
REMOTE DEVICE

Fig. 1

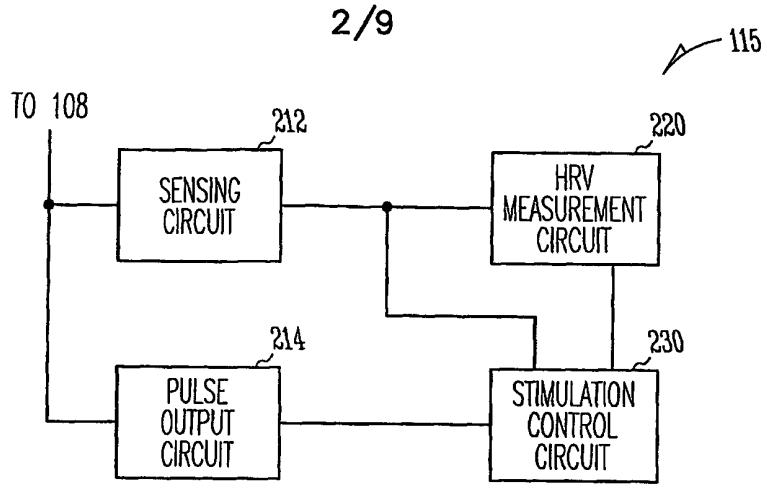

Fig. 2

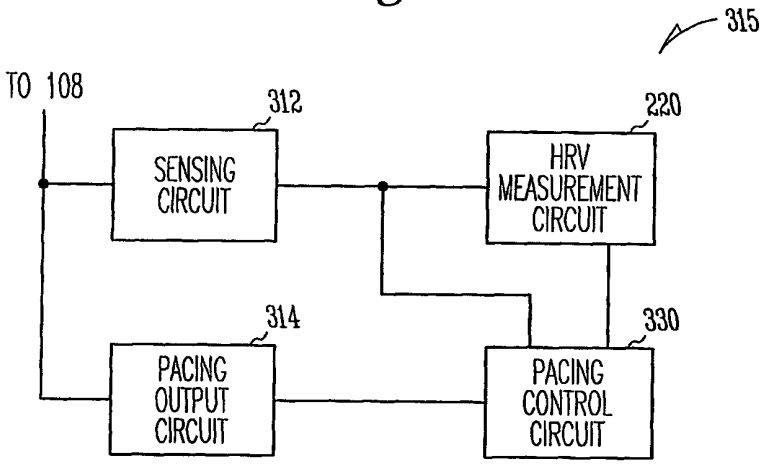

Fig. 3

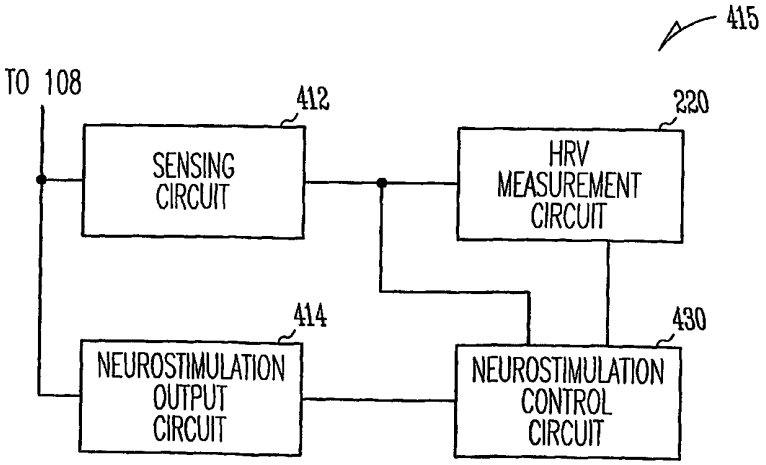

Fig. 4

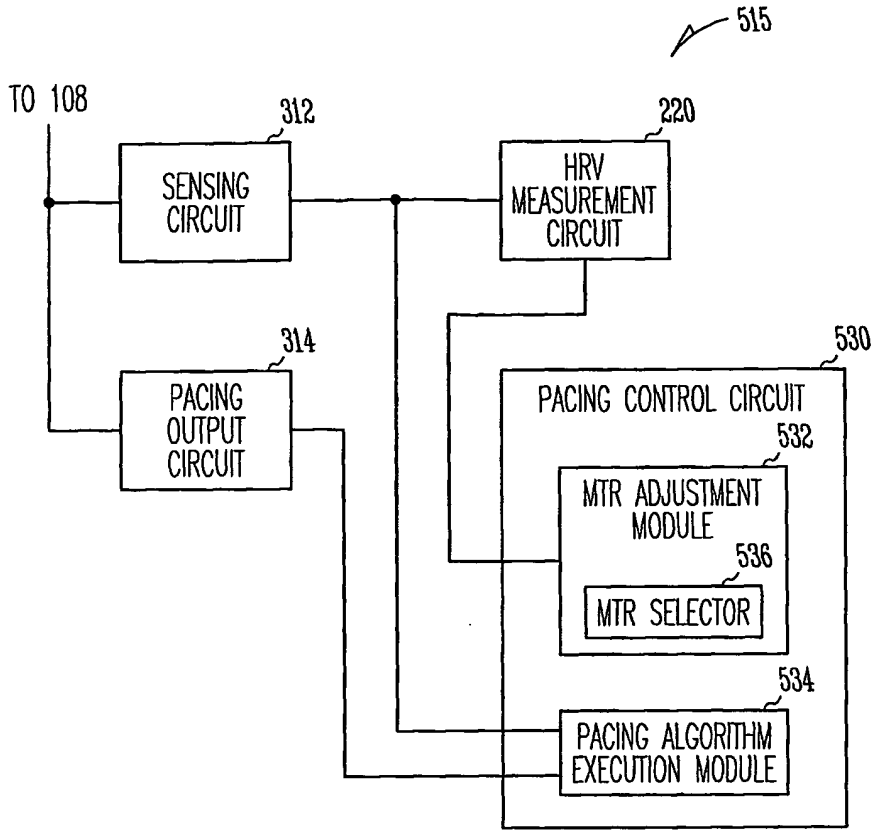
515
TO 108
312
SENSING CIRCUIT
220
HRV MEASUREMENT CIRCUIT
314
PACING OUTPUT CIRCUIT
530
PACING CONTROL CIRCUIT
532
MTR ADJUSTMENT MODULE
536
MTR SELECTOR
534
PACING ALGORITHM EXECUTION MODULE

Fig. 5

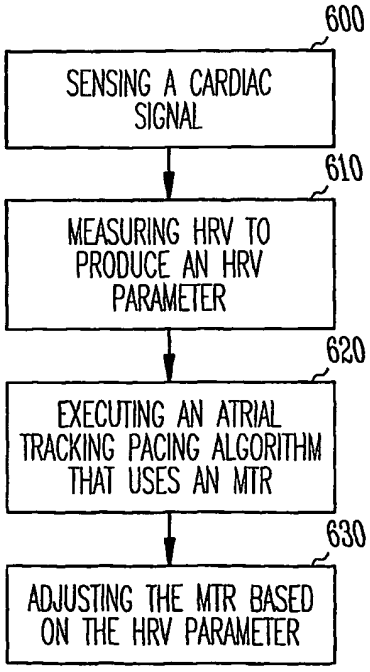
600
SENSING A CARDIAC SIGNAL
610
MEASURING HRV TO PRODUCE AN HRV PARAMETER
620
EXECUTING AN ATRIAL TRACKING PACING ALGORITHM THAT USES AN MTR
630
ADJUSTING THE MTR BASED ON THE HRV PARAMETER

Fig. 6

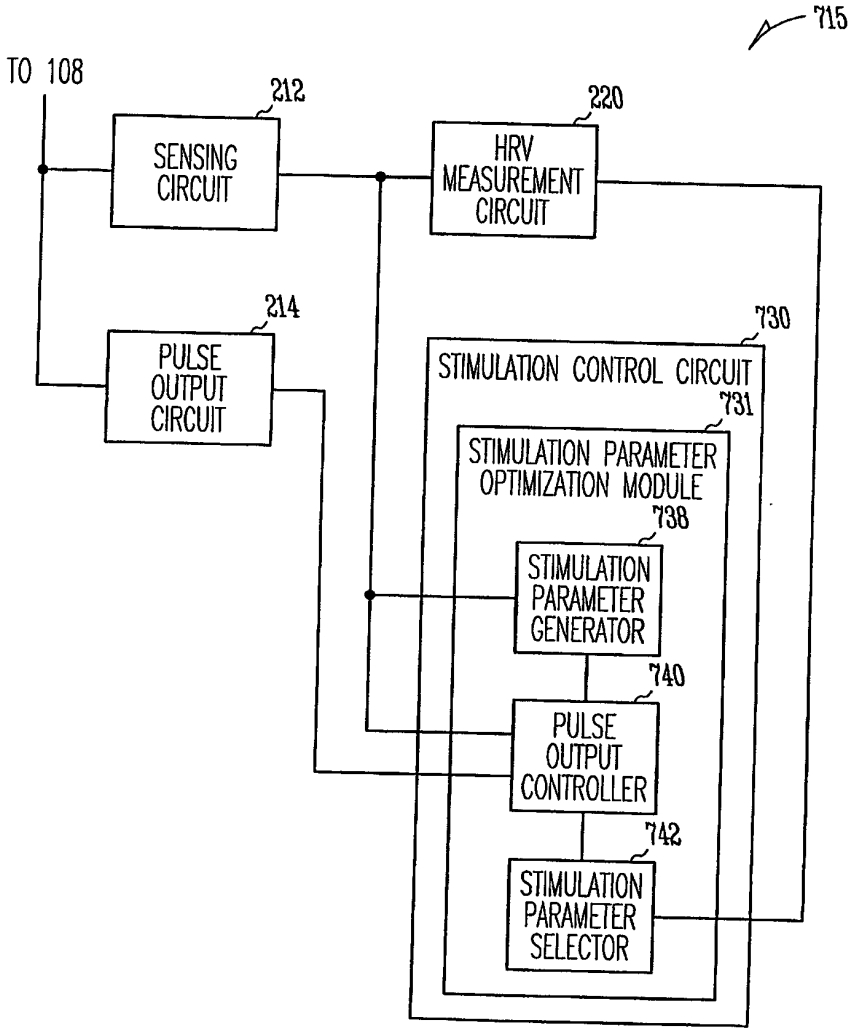
715
TO 108
212
SENSING CIRCUIT
220
HRV MEASUREMENT CIRCUIT
214
PULSE OUTPUT CIRCUIT
730
STIMULATION CONTROL CIRCUIT
731
STIMULATION PARAMETER OPTIMIZATION MODULE
738
STIMULATION PARAMETER GENERATOR
740
PULSE OUTPUT CONTROLLER
742
STIMULATION PARAMETER SELECTOR

Fig. 7

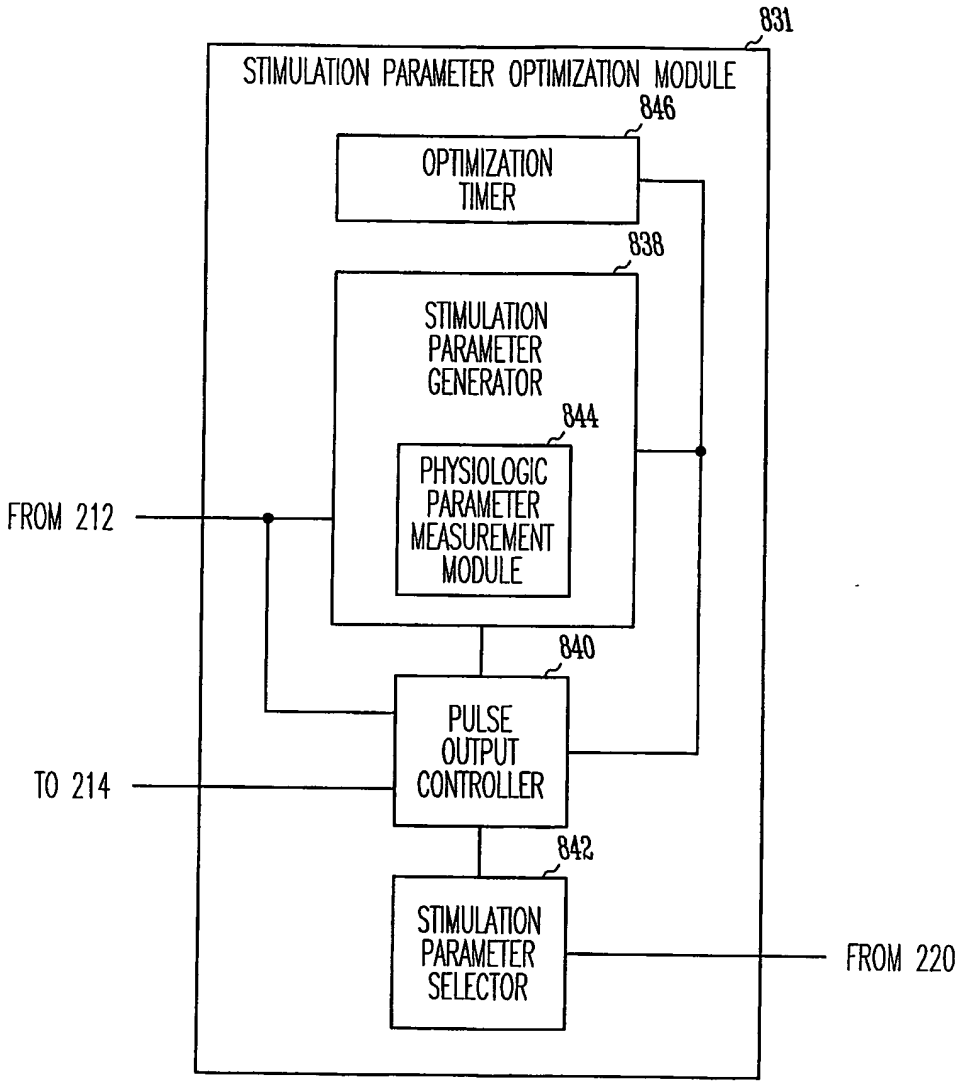
831
STIMULATION PARAMETER OPTIMIZATION MODULE
846
OPTIMIZATION TIMER
838
STIMULATION PARAMETER GENERATOR
844
PHYSIOLOGIC PARAMETER MEASUREMENT MODULE
FROM 212
840
PULSE OUTPUT CONTROLLER
TO 214
842
STIMULATION PARAMETER SELECTOR
FROM 220

Fig. 8

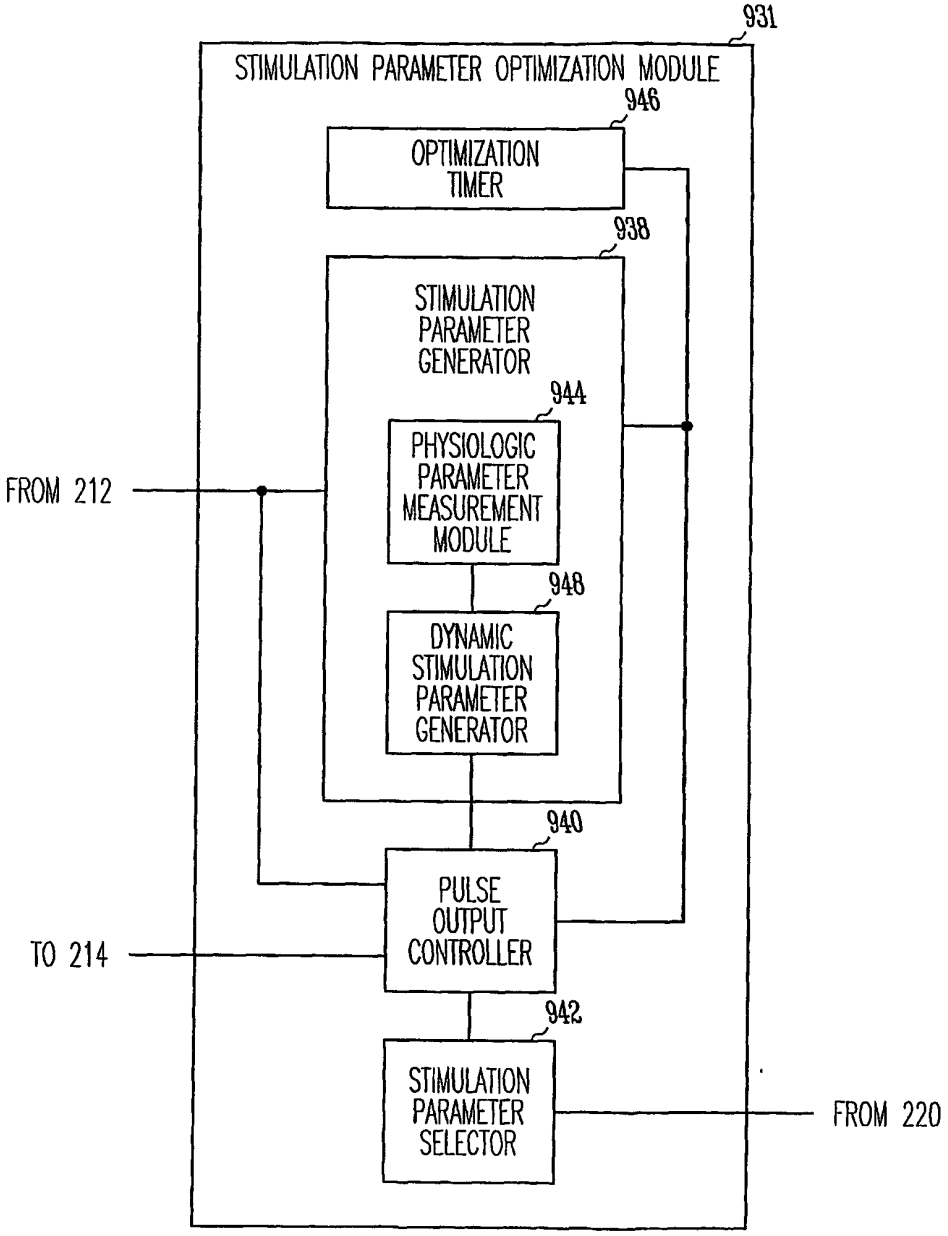
931
STIMULATION PARAMETER OPTIMIZATION MODULE
946
OPTIMIZATION TIMER
938
STIMULATION PARAMETER GENERATOR
944
PHYSIOLOGIC PARAMETER MEASUREMENT MODULE
948
DYNAMIC STIMULATION PARAMETER GENERATOR
940
PULSE OUTPUT CONTROLLER
942
STIMULATION PARAMETER SELECTOR
FROM 212
TO 214
FROM 220

Fig. 9

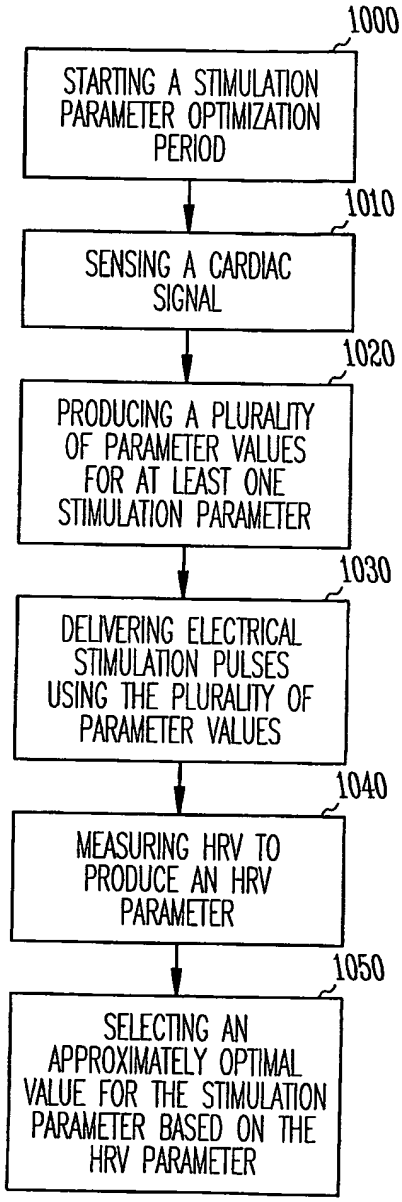
1000
STARTING A STIMULATION PARAMETER OPTIMIZATION PERIOD
1010
SENSING A CARDIAC SIGNAL
1020
PRODUCING A PLURALITY OF PARAMETER VALUES FOR AT LEAST ONE STIMULATION PARAMETER
1030
DELIVERING ELECTRICAL STIMULATION PULSES USING THE PLURALITY OF PARAMETER VALUES
1040
MEASURING HRV TO PRODUCE AN HRV PARAMETER
1050
SELECTING AN APPROXIMATELY OPTIMAL VALUE FOR THE STIMULATION PARAMETER BASED ON THE HRV PARAMETER

Fig. 10

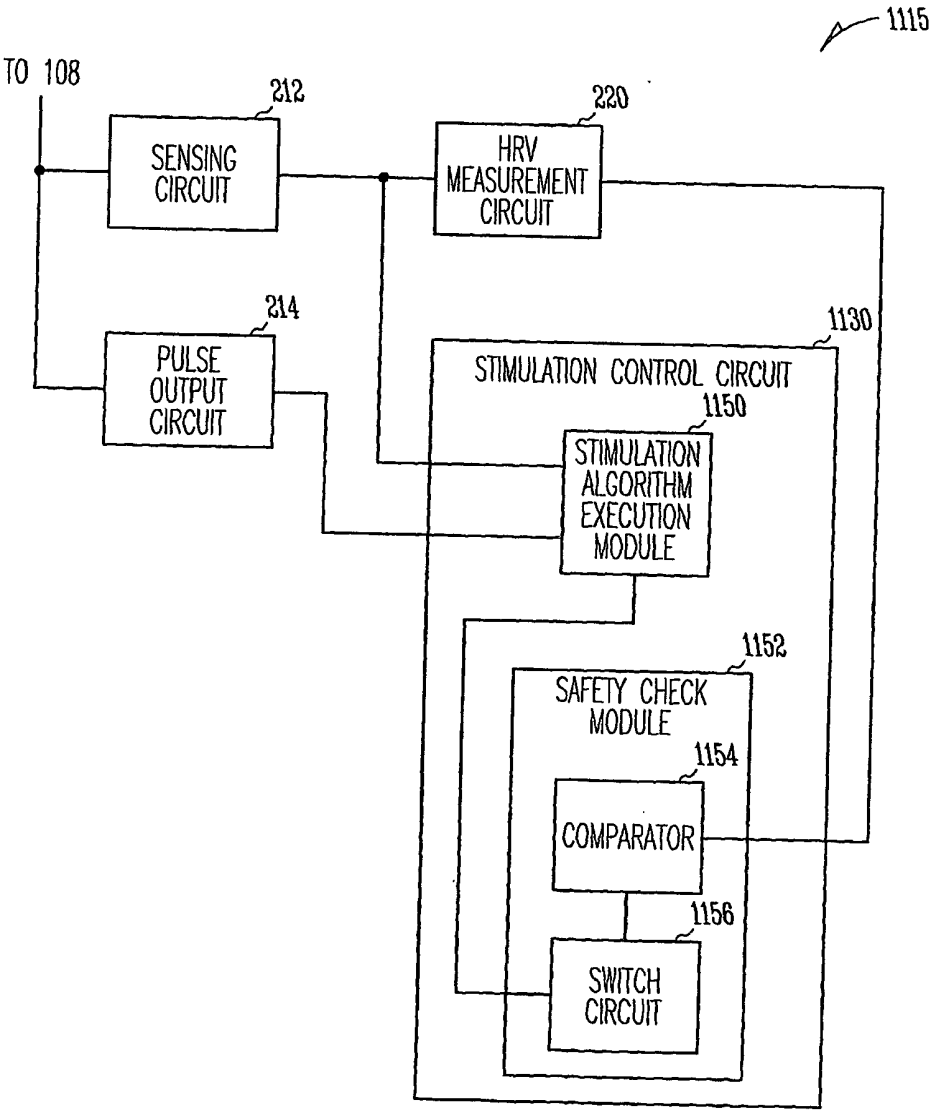
1115
TO 108
212
SENSING CIRCUIT
220
HRV MEASUREMENT CIRCUIT
214
PULSE OUTPUT CIRCUIT
1130
STIMULATION CONTROL CIRCUIT
1150
STIMULATION ALGORITHM EXECUTION MODULE
1152
SAFETY CHECK MODULE
1154
COMPARATOR
1156
SWITCH CIRCUIT

Fig. 11

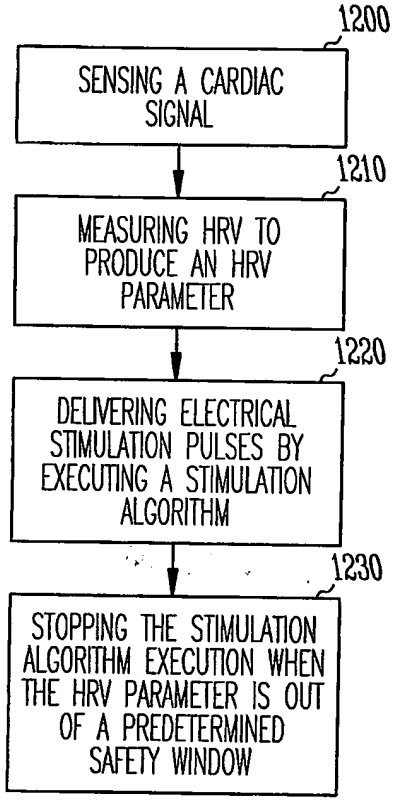
1200
SENSING A CARDIAC SIGNAL
1210
MEASURING HRV TO PRODUCE AN HRV PARAMETER
1220
DELIVERING ELECTRICAL STIMULATION PULSES BY EXECUTING A STIMULATION ALGORITHM
1230
STOPPING THE STIMULATION ALGORITHM EXECUTION WHEN THE HRV PARAMETER IS OUT OF A PREDETERMINED SAFETY WINDOW

Fig. 12

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